## We claim:

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- 1. A method for identifying chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype comprising administration of a test compound and a chemotherapeutic agent to which cancer cells are resistant and measuring cancer cell survival.
- 2. A method for resensitizing non P-gr/non MRP multiple drug resistant cancer cells to treatment with chemotherapeutic agents to which cancer cells have developed resistance comprising administration of an effective amount of a chemosensitizing reversal agent and a chemotherapeutic agent.
- 3. The method according to claim 2 wherein the chemosensitizing reversal agent is selected from the group consisting of fumitremorgin A, fumitremorgin B and fumitremorgin C.
- 4. The method according to claim 2 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
- 5. The method according to claim 2 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin and topotecan.
- 6. The method of claim 3 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
- 7. A method for identifying chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells which exhibit BCRP-mediated multiple drug resistance comprising administration of a test compound and a chemotherapeutic agent to which the cancer cells are resistant and measuring cancer cell survival.
- 8. A method for resensitizing BCRP-mediated multiple drug resistant cancer cells to treatment with chemotherapeutic agents to which cancer cells have developed resistance comprising administration of an effective amount of a chemosensitizing reversal agent and a chemotherapeutic agent.
- 9. The method according to claim 8 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.

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- 10. The method according to claim be wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin, and topotecan.
- 11. The method according to claim 8 wherein the chemosensitizing reversal agent is selected from the group consisting of furnitremorgin A, furnitremorgin B and furnitremorgin C.
- 12. The method according to claim 11 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
  - 13. A method of distinguishing P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance which comprises administration of an effective amount of a chemosensitizing reversal agent and a chemotherapeutic agent to which cancer cells are resistant and measuring cancer cell survival.
  - 14. The method according to claim 13 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
  - 15. The method according to claim 13 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorub cin, and topotecan.
  - 16. The method according to claim 13 wherein the chemosensitizing reversal agent is selected from the group consisting of fumitremorgin A, fumitremorgin B and fumitremorgin C.
  - 17. The method according to claim 16 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
  - 18. A method of distinguishing P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance which comprises administration of an effective amount of a chemosensitizing reversal agent and a chemotherapeutic agent to which the cancer cells are multiple drug resistant and measuring chemotherapeutic agent accumulations in the cell.

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- 19. The method according to claim 18 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
- 20. The method according to claim 18 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin, and topotecan.
  - 21. The method according to claim 18 wherein the chemotherapeutic agent is substituted by a drug surrogate.
- 15 22. The method according to claim 18 wherein the chemosensitizing reversing agent is selected from the group consisting of furnitremorgin A, furnitremorgin B and furnitremorgin C.
  - 23. The method according to claim 22 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
  - 24. A method of determining the presence and magnitude of cancer cell BCRP or other non P-gp/non MRP resistance in cancer cells exhibiting such resistance which comprises administration of an effective amount of a chemosensitizing reversal agent and chemotherapeutic agents to resistant cancer cells from humans and measuring cancer cell survival.
  - 25 The method according to claim 24 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
    - 26. The method according to claim 24 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin, and topotecan.
- 27. The method according to claim 24 wherein the chemosensitizing reversal agent is selected from the group consisting of fumitremorgin A, fumitremorgin B and fumitremorgin C.
- 28. The method according to claim 27 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.

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- 29. A method of reversing BCRP of other non P-gp/non MRP resistance to chemotherapeutic agents in a mammal which comprises administration of an effective amount of a chemosensitizing reversal agent to a mammal in need thereof having a BCRP or other non-P-gp/non MRP resistant cancer.
- 30. The method according to claim 29 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
- 31. The method according to claim 29 wherein the chemotherapeutic agent is selected from 15 the group consisting of mitoxantrone, doxorubicin, and topotecan.
  - 32. The method according to claim 29 wherein the chemosensitizing reversal agent is selected from the group consisting of fumitremorgin A, fumitremorgin B and fumitremorgin C.
  - 33. The method according to claim 32 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
  - 34. A method of treatment of BCRP or other non P-gp/non MRP multiple drug resistant phenotype cancer cells which comprises administration of an effective amount of a chemosensitizing reversal agent and a chemotherapeutic agent to which the cancer is resistant.
    - 35. The method according to claim 34 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
    - 36. The method according to claim 34 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin, and topotecan.
    - 37. The method according to claim 34 wherein the chemosensitizing reversal agent is selected from the group consisting of fumitremorgin A, fumitremorgin B and fumitremorgin C.



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- 38. The method according to claim 37 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
- 39. The method of inhibiting efflux of a chemotherapeutic agent in a mammal in need thereof which comprises administration of an effective amount of a chemosensitizing reversal agent and a chemotherapeutic agent to which the cancer is resistant.
- 40. The method according to claim 39 wherein the chemotherapeutic agent used is one to which the cancer cells show resistance to the BCRP or other non P-gp/MRP-mediated phenotype.
- 41. The method according to claim 39 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin, and topotecan.
- 42. The method according to claim 39 wherein the chemosensitizing reversal agent is selected from the group consisting of furnitremorgin A, furnitremorgin B and furnitremorgin C.
  - 43. The method according to claim 42 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
  - 44. A compound having the Formula (I)

    R

    R

    R

    R

    R

    R

    (I)

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wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms; R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms; R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms, R<sup>7</sup>NH(CH2)v- or

m is an integer of 1 to 6;

v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

 $R^{7}$  is H or

 $R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $-(CH_2)_mCO_2H$ ,

and

with the proviso that n is not 1 when

 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

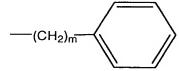
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or

and

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- 5 R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; or a pharmaceutically acceptable salt thereof.
  - 45. A compound according to claim \$4 wherein
- R<sup>1</sup> is hydrogen or alkoxy of 1 to 5 carbon atoms;
  R<sup>2</sup> is hydrogen or alkenyl of 2 to 6 carbon atoms;
  R<sup>3</sup> is hydrogen, alkyl of 1 to 9 carbon atoms, alkenyl of 2 to 6 carbon atoms,
  R<sup>7</sup>NH(CH2)v- or



m is an integer of 1 to 5; v is an integer of 1 to 3;

or a pharmaceutically acceptable salt thereof.

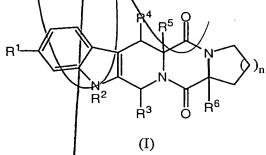
46. A compound according to claim 44 wherein R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are are independently (R) or (S); or a pharmaceutically acceptable salt thereof.

- 47. A compound according to claim 44 wherein R¹ is hydrogen or CH₃O-;
  R² is hydrogen or 3-methyl-2-buten-1-yl;
  R³ is hydrogen or (R) or (S) 2-methyl propyl, 2-methyl-2-propenyl, nonanyl, 5-phenylpentyl, or R³NHCH₂CH₂CH₂- where R³ is hydrogen, acetyl, butyryl, succinoyl, or 3-(2-pyrrolidinyl)propionyl;
  R⁴ and R⁵ independently are (R) or (S) hydrogen;
  or a pharmaceutically acceptable salt thereof.
- 48. The compound of claim 44 which is selected from the group consisting of (5aS,12R,14aR)-12-isobutyl-1,2,3,5a,6,11,12,14a-octahydro-5H,14H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione, (5aS,12S,14aR)-12-isobutyl-1,2,3,5a,6,11,12,14a-octahydro-5H,14H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione,

(5aR,12R,14aR)-12-isobutyl-1,2,3,5a,6,11,12,14a-octahydro-5H,14H-5 pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione, (5aR, 12S, 14aR)-12-isobutyl-1,2,3,5a,6, $\sqrt{1}$ ,12,14a-octahydro-5H,14Hpyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione, (6aS,13R,15aS)-13-isobutyl-1,2,3,4,6a,7,12,13,15a-nonahydro-6H,15H-10 pyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (6aS,13S,15aS)-13-isobutyl-1,2,3,4,6a,7,12,13,15a-nonahydro-6H,15Hpyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (6aR,13R,15aS)-13-isobutyl-1,2,3,4,64,7,12,13,15a-nonahydro-6H,15Hpyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, 15 (6aR,13S,15aS)-13-isobutyl-1,2,3,4,64,7,12,13,15a-nonahydro-6H,15Hpyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (6aS,13R,15aR)-13-isobutyl-1,2,3,4,6a,7,12,13,15a-nonahydro-6H,15Hpyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (6aS,13S,15aR)-13-isobutyl-1,2,3,4,6a,7,12,13,15a-nonahydro-6H,15H-20 pyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (6aR,13R,15aR)-13-isobutyl-1,2,3,4,6a,7,12,13,15a-nonahydro-6H,15Hpyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (6aR,13S,15aR)-13-isobutyl-1,2,3,4,6a,7,12,13,15a-nonahydro-6H,15Hpyrido[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-6H,15H-dione, (4aS,11R,13aS)-11-isobutyl-1,4a,5,10,11,13a-hexahydro-4H-25 azeto[1",2":4',5']pyrazino[2',1':6,1/pyrido[3,4-b]indole-4,13(2H)-dione, (4aS,11S,13aS)-11-isobutyl-1,4a,5,10,11,13a-hexahydro-4Hazeto[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-4,13(2H)-dione, (5aS,12R,14aS)-12-(5-phenylpentyl)-1,2,3,5a,6,11,12,14a-octahydro-5H,14Hpyrrolo[1",2":4',5']pyrazino[2,1':6,1]pyrido[3,4-b]indole-5,14-dione, 30 (5aS,12S,14aS)-12-(5-phenylpentyl)-1,2,3,5a,6,11,12,14a-octahydro-5H,14Hpyrrolo[1",2":4',5']pyrazino[2\,1':6,1]byrido[3,4-b]indole-5,14-dione; benzyl 3-[(5aS,12R,14aS)-5,14-dioxof2,3,5a,6,11,12,14,14a-octahydro-1H,5Hpyrrolo[1",2":4',5']pyrazino[2',\\daggerightarrologianity. 12-yl]propylcarbamate, benzyl 3-[(5aS,12S,14aS)-5,14-dioxo-2,3,5a,6,11,12,14,14a-octahydro-1H,5H-35 pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indol-12-yl]propylcarbamate. (5aS,14aS)-1,2,3,5a,6,11,12,14a-octalydro-5H,14Hpyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione, (5aS,12S,14aS)-12-methyl-1,2,3,5a,6, 1,12,14a-octahydro-5H,14H-

pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione,

- 5 (5aS,12S,14aS)-12-nonyl-1,2,3,5a,6,11,12,14a-octahydro-5H,14H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione, (5aS,12R,14aS)-12-(3-aminopropyl)-1,2,3,5a,6,11,12,14a-octahydro-5H,14H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione, (5aS,12S,14aS)-12-(3-aminopropyl)-1,2,3,5a,6,11,12,14a-octahydro-5H,14H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione
- pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione,
  N-{3-[(5aS,12S,14aS)-5,14-dioxo-2,3,5a,6,11,12,14,14a-octahydro-1H,5H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indol-12-yl]propyl}acetamide,
  N-{3-[(5aS,12S,14aS)-5,14-dioxo-2,3,5a,6,11,12,14,14a-octahydro-1H,5H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indol-12-yl]propyl}butanamide,
- 4-({3-[(5aS,12S,14aS)-5,14-dioxo-2,3|5a,6,11,12,14,14a-octahydro-1H,5H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indol-12-yl]propyl}amino)-4-oxobutanoic acid,
  - (2S)-N-{3-[(5aS,12S,14aS)-5,14-dioko-2,3,5a,6,11,12,14,14a-octahydro-1H,5H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indol-12-yl]propyl}pyrrolidine-2-carboxamide and
  - (5aS,12S,14aS)-9-methoxy-11/(3-methylbut-2-enyl)-12-(2-methylprop-1-enyl)-1,2,3,5a,6,11,12,14a-octahydro-5H, 4H-pyrrolo[1",2":4',5']pyrazino[2',1':6,1]pyrido[3,4-b]indole-5,14-dione or a pharmaceutically acceptable salt thereof.
  - 49. A pharmaceutical composition for resensitizing multiple drug resistant chemotherapeutic agents which comprises a compound of Formula (I)



- 30 wherein:
  - n is an integer of 0, 1, or 2;
  - R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;
  - R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;
  - R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,
- 35  $R^7NH(CH2)v-$  or

—(CH<sub>2</sub>)<sub>m</sub>

m is an integer of 1 to 6; v is an integer of 1 to 4; R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

10 R<sup>7</sup> is H or

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R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,

-O-CH<sub>2</sub> and

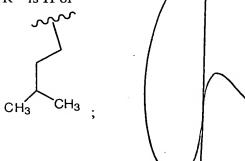
 $-(CH_2)_m$ 

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with the proviso that n is not I when

 $R^1$  is  $\hat{H}$  or  $CH_3O$ -;

20 R<sup>2</sup> is H or



R<sup>3</sup> is

$$CH_3$$
  $CH_3$   $CH_3$   $CH_3$  ; and

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R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

50. A method of treating multiple drug resistance in a mammal in need thereof, which comprises administering to said mammal, a chemotherapeutic agent and an effective amount of a chemosensitizing reversal agent of Formula (I)

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wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH2)v- or

m is an integer of 1 to 6;

v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

 $R^7$  is H or

R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,

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$$-CH_2$$
 and  $-(CH_2)_m$ 

with the proviso that n is not 1 when

 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

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 $R^3$  is  $CH_3$   $CH_3$   $CH_3$   $CH_3$   $CH_3$   $CH_3$ 

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

- or a pharmaceutically acceptable salt thereof; said chemosensitizing reversal agent being administered in an effective amount to increase the sensitivity of the chemotherapeutic agent to the multiple drug resistant cancer.
- 51. The method of claim 50 wherein the multiple drug resistant cancer is non P-gp/non MRP.
  - 52. The method of claim 50 wherein the multiple drug resistant cancer expresses BCRP.
  - 53. The method of claim 50 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin and topotecan.
- 54. The method according to claim 50 wherein the chemotherapeutic agent used is one to which the cancer cells are resistant.
  - 55. The method according to claim 2 wherein the chemosensitizing reversal agent is a compound having the Formula (I)

wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

10 R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH2)v- or

m is an integer of 1 to 6;

v is an integer of 1 to 4;

 $R^4$ ,  $R^5$  and  $R^6$  are hydrogen;

 $R^7$  is H or

20 R<sup>8</sup> is selected from alkylof 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,

$$-O-CH_2$$
 and  $-(CH_2)_m$ 

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with the proviso that n is not it when

 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

or  $CH_3$   $CH_3$ 

and

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; or a pharmaceutically acceptable salt thereof.

56. The method according to claim 8 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)

wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

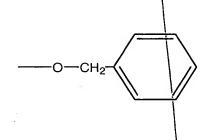
R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH2)v- or

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- m is an integer of 1 to 6;
  - v is an integer of 1 to 4;
  - R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;
  - $R^7$  is H or
- R<sup>8</sup> is selected from a kyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H, 10

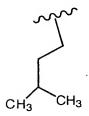


and

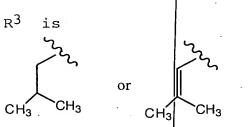
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with the proviso that n is not 1 when

- $R^1$  is H or  $CH_3O$ -;
- $R^2$  is H or



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- R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; or a pharmaceutically acceptable salt thereof.
  - 57. The method according to claim 13 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)

and

$$\begin{array}{c|c}
 & R^4 & R^5 & O \\
 & R^2 & R^3 & O & R^6
\end{array}$$
(I)

wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1\to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms; 10

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

 $R^7NH(CH2)v-or$ 

m is an integer of 1 to 6; 15

v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

 $R^7$  is H or

 $R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $\text{-(CH}_2)_{m}\text{CO}_2\text{H}\text{,}$ 20

and

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with the proviso that n is not 1 when

 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

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R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

or a pharmaceutically acceptable salt thereof.

58. The method according to claim 18 wherein the chemosensitizing reversing agent is selected from a compound having the Formula (I)

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
N & N & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
R^6 & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
R^6 & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
R^6 & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
R^6 & N & N
\end{array}$$

$$\begin{array}{c|c}
R^4 & R^5 & O \\
R^6 & N & N
\end{array}$$

wherein:

n is an integer of 0, 1, or 2;

- R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;
- R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;
- $R^3$  is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH2)v- or

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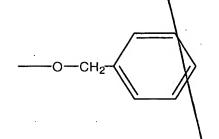
m is an integer of 1 to 6;

- v is an integer of 1 to 4;
  - R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;
  - $R^7$  is H or



 $R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $-(CH_2)_mCO_2H$ ,

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and

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- with the proviso that n is not 1 when
- $R^1$  is H or  $CH_3O$ -;
- $R^2$  is H or

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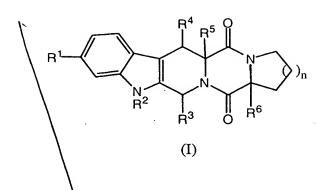
 $R^3$ 

or

CH<sub>3</sub>

- R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;
- or a pharmaceutically acceptable salt thereof. 25
  - 59. The method according to claim 24 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)

and



wherein:

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MA CPEAD

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n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

 $\mathbb{R}^3$  is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH2)v- or

m is an integer of 1 to 6;

v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

 $R^7$  is H or

 $R^8$  is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H, 20

with the proviso that n is not 1 when

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$$CH_3$$
  $CH_3$   $CH_3$ 

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; or a pharmaceutically acceptable salt thereof.

60. The method according to claim 29 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)

and

$$\begin{array}{c|c}
R^4 & R^5 & \\
N & N & N \\
N & N & N
\end{array}$$
(I)

wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms, R<sup>7</sup>NH(CH2)v- or

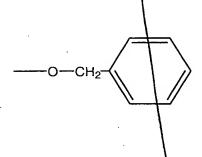
m is an integer of 1 to 6;

- 5 v is an integer of 1 to 4;
  - R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

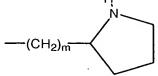
 ${\tt R}^7\ \ \text{is H or}$ 



R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,



and



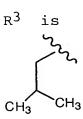
with the proviso that n is not 1 when

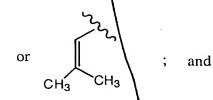
 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

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R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

- or a pharmaceutically acceptable salt thereof.
- 61. The method according to claim 34 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



wherein:

n is an integer of 0, 1, or 2;

 $\mathbb{R}^1$  is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH2)v- or

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m is an integer of 1 to 6;

v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

 $R^7$  is H or

20

 $R^8$  is selected from alkyl of 1 to 10 carbon atoms  $-(CH_2)_mCO_2H$ ,

and

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with the proviso that n is not 1 when

 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

15

20

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CH<sub>3</sub> CH<sub>3</sub>

 $\mathbb{R}^3$  is or  $\mathbb{C}H_3$   $\mathbb{C}H_3$   $\mathbb{C}H_3$  and

 $R^4,\,R^5\,$  and  $R^6$  are hydrogen; or a pharmaceutically acceptable salt thereof.

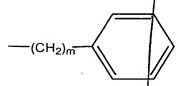
62. The method according to claim 39 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)

wherein:

n is an integer of 0/1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms; R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1/to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms, R<sup>7</sup>NH(CH2)v- or

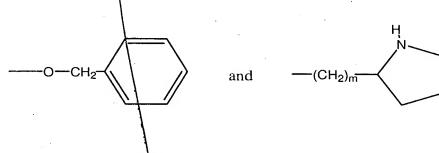


m is an integer of 1 to 6;

v is an integer of 1 to 4; R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; R<sup>7</sup> is H or

R<sup>8</sup>:

R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,



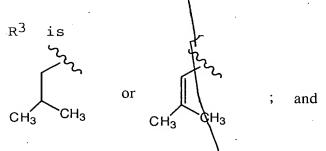
with the proviso that n is not 1 when

 $R^1$  is H or  $CH_3O$ -;

 $R^2$  is H or

20

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 $R^4$ ,  $R^5$  and  $R^6$  are hydrogen;

or a pharmaceutically acceptable salt thereof.

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63. A culture of the organism *Aspergillus fumigatus* having the identifying characteristics of LL-S266, said culture being capable of producing Fumitremorgin A, B and C in recoverable quantity upon fermentation in an aqueous nutrient medium containing assimilable sources of carbon and narrogen.